

BRITISH HEART JOURNAL

Foreword

Atherosclerosis

It is likely that more than 90% of the facts about the processes involved in atherosclerosis are now known. What is far less certain is how these facts can be fitted into an overall framework in order to understand fully the pathogenesis and progression of the disease.

Atherosclerosis is a very old disease, which has been found in the mummies of Egyptian pharaohs. But it was not until the latter half of this century that the disease became established as the cause of more than 50% of deaths. It is unlikely that this change can be explained solely by the greater lifespan achieved by the control of epidemic infectious disease. Part of the answer may lie in a qualitative change within the plaque that increases the risk of thrombosis, and thus would account for much of the mortality of the disease.

The relation between the lipid content of plaques and the risk of thrombosis is considered by Davies and Woolf in the first article in this supplement. The concept that thrombosis is responsible both for clinically expressed acute ischaemic episodes and the clinically silent progression of coronary stenoses is explored.

Witztum considers a paradox, now explained, that had bedevilled the subject for years. Plasma low density lipoprotein freely enters and leaves intima. It is not taken up by macrophages, yet a vital component of atherogenesis is lipid uptake by macrophages. The answer lies in oxidation of the lipid which enables it to be taken up specifically by the "scavenger" receptor.

Faruqui and DiCorleto, Raines and Ross, and Hansson describe the cell biology of the monocyte, smooth muscle cell, and lymphocyte within the plaque. The tremendous explosion in the knowledge of interactions between the different cell types in the plaque through cytokines and growth factors has probably now reached a plateau and thoughts turn toward therapeutic modulation of the processes. The success or failure of some of these attempts will indicate which particular processes are important in atherogenesis. The therapeutic options are reviewed by Cleland and Krikler.

Holme reviews the evidence about the clinical benefit of a reduction in lipid concentrations, with a timely reminder of the complexities of meta-analysis. Brown and his colleagues review the first attempts at modification of atherosclerosis by drugs. There are grounds for a modest degree of optimism. Judged by the reduction in the number of episodes of acute ischaemia after therapy or by sequential angiography the progress of the disease can be modified in subjects who have already declared that they have coronary atherosclerosis.

It is too early to translate this modest optimism into full-scale drug intervention in patients who have not already declared (by having angina or infarction) that they are at high risk. The current therapeutic guidelines suggested by Cobbe and Shepherd emphasise the importance of secondary prevention. Whether lowering lipid concentrations influences morbidity rather than mortality in primary prevention is discussed by Castelli. He robustly expresses the opinion that even if mortality were not altered, the influence of lipid reduction on morbidity is of great importance. To pass through life happily is as valuable as total lifespan.

The stage is set for trials of a number of drugs that either alter plasma lipid concentrations to a far greater extent than previous drugs or have entirely different actions—for example, antioxidants to prevent lipid modification within the intima. This supplement aims to explain for practising clinical cardiologists why these drugs may be effective.

The supplement as a whole has been supported by an educational grant from the Medical Sciences Liaison Division of the Upjohn Company to the *British Heart Journal*. The supplement conforms with the British Medical Association guidelines for such support.

M J DAVIES
Editor

British Heart Journal,
9 Fitzroy Square,
London W1P 5AH